

Medical membrane for stimulating tissue formation

Cross References to Related Applications

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This application claims the priority of German patent application No. 199 26 438.4, filed June 10, 1999 and of German patent application No. 199 48 787.1, filed October 10, 1999 the disclosure of which is incorporated herein by reference in its entirety.

Technical Field

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The present application relates to a medical membrane as well as to a method for the application of a medical membrane in dentistry.

Background Art

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In the context of healing processes medical membranes allow a selective influence on cell types with different growth rates and attachment characteristics, respectively, which are available in the wound area. Undesired cell types with higher growth rates are e.g. hindered to invade the wound area and the attachment of cells which form the new tissue is stimulated. This method is referred to as "guided tissue regeneration". The term "guided bone regeneration" is used if the application of medical membranes selectively hinders fast growing epithelium cells and connective tissue cells to invade the wound area and to proliferate therein and thereby enables slow growing bone cells to heal the tissue defect.

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Medical membranes are made of various materials. Reabsorbable membranes are made of collagen or polylactic/polyglycolide acid polymer or copolymer, re-

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spectively. Non-reabsorbable membranes are made of polytetrafluorethylene. Reabsorbable membranes remain in situ; non-reabsorbable membranes are removed after completion of their task.

5 Studies have shown that medical membranes which were developed in wound repair studies e.g. collagen or polytetrafluorethylene can stimulate the attachment and integration of fibroblasts or other cells forming new tissue as well as wound closure.

10 Furthermore, in vitro as well as in vivo studies have shown the importance of mechanical stability, sterility and absence of inflammation for the preservation of the pulp after its exposure by a trauma or in the context of restorative measures or partial resection,
15 respectively. In order to preserve the vitality of the pulp it is as well important to avoid the formation of a cavity below the filling due to shrinkage of the blood clot and to avoid a wound treatment harming the pulp and it is important to achieve a bacteria impermeable sealing
20 of the dentine wound. Nowadays most often applied method is to produce a scurf of the pulp and said method is very harmful to the pulp and to its ability to regenerate and therefore new means are needed which allow a less harmful pulp treatment.

25 The present invention has the aim to provide means in order to improve the preservation of the pulp vitality.

Disclosure of the Invention

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Said aim is accomplished by a medical membrane according to claim 1.

Hence, it is a general object of the invention to provide a medical membrane for the arrangement in
35 a cavity of the dentine of a tooth for the capping of a pulpal wound. It is shown that due to the protection of the membrane the ability of the pulp to regenerate and

its vitality is improved. Besides direct pulp exposures, deep dentine wounds are generated by injuring dentine channels which leads to a serious burden for the pulp and the pulp is injured in this way.

5 A membrane which is essentially impermeable to a sealant or for a cement is preferred. The term "essentially impermeable" means that the membrane is impermeable to substances which can disturb the pulp regeneration and/or dentine regeneration.

10 Preferred is a membrane which comprises at least one roughened surface allowing the attachment of fibrin fibers, the attachment and ingrowth of pulpal fibroblasts and of other cells.

15 In a preferred embodiment the roughened surface has a porous and/or reticular structure. However, said porous and/or reticular structure of the membrane allows diffusion of molecules and ions through the membrane. On the one hand the membrane comprises a roughened surface which has preferably a porous and/or reticular
20 structure, on the other hand said membrane is at least impermeable to substances disturbing the pulp regeneration to protect the pulp. This can e.g. be achieved by a bilayer design. Said bilayer design is characterized by a denser structure of the membrane side facing away from
25 the pulp and thereby impermeability of the membrane is obtained. In a further embodiment, diffusion of harmful substances is prevented by an uniformly structured membrane wherein the side of said membrane facing away from the pulp comprises a differently structured, in particu-
30 lar an impermeable layer or coating. However, said membrane has to be so impermeable to prevent at least temporarily diffusion of substances disturbing pulp regeneration or dentine regeneration so that an impermeable sealing, preferably a hardening coating, after application of
35 the membrane is possible.

 In order to facilitate anchorage of fibrin fibers and ingrowth of fibroblasts or other regenerative

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cells it is proposed that the percentage of the pores or of the mesh of the porous or reticular surface which is in contact with the pulp is higher than 20%, preferably higher than 50%. The percentage of pores or the mesh, respectively, promotes attachment and integration of regenerative cells and thereby provides wound healing and the vitality of the pulp is preserved, preferably followed by a curing material which closes the pulp exposure.

A particular good integration of regenerative cells is seen if the average diameter of the pores or the width of the mesh lies between 0.5 μm and 200 μm , preferably between 1 μm and 100 μm .

Preferred is a membrane which is self adhesive to the dental hard tissues or which due to an adhesive coating is adhesive to the dental hard tissues without harming the pulp so that the sealant which preferably shows adhesion to the dental hard tissues such as e.g. glassionomer cement or light hardening glassionomer cement, is neither in direct nor indirect contact with the pulp due to the impermeability of the membrane.

The medical membrane according to the present invention forms per se or preferably after sealing with a hardening material or after coating, respectively, a preferably hard and impermeable barrier on the one hand between the pulp exposure and adjacent dental hard tissues and on the other hand between the restorative material above the sealed or coated membrane wherein said restorative material partially or fully replaces the missing dental hard tissues. The impermeability of the membrane which said membrane shows per se or which is achieved by overlaying the membrane with a restorative material provides for that substances neither can diffuse from the pulp to the restorative material nor from the restorative material to the pulp. Therefore, the membrane is either per se or after overlaying with restorative material impermeable to the penetration of liquids such as blood, serum and water. In addition, the membrane is bio-

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logically impermeable to cells and microorganisms and where required for the biocompatibility the membrane is chemically impermeable to molecules and ions disturbing the pulp regeneration and dentine regeneration.

5 Preferred is a membrane which has a surface of less than 100mm^2 , preferably less than 50mm^2 . The nowadays available size units of medical membranes are not only due to lack of adhesion, thickness and impermeability unsuitable for the capping of a pulp wound. In
10 practice, this kind of membranes can as well not be cut to the appropriate size since the membranes have to be very small and sterile and thus the cutting of an opened membrane to the appropriate size and its adaptation increases the risk for infections which is not acceptable.
15 The remaining pieces of the expensive membranes can not be stored for sterility reasons.

Only the construction of known medical membranes or dental membranes, respectively, as membrane pads in an applicable form enables their use in pulp re-
20 generation and dentine regeneration. Said membranes open via guided cell proliferation and formation of new tissues a new field which as "guided pulp regeneration" or "guided dentine regeneration", respectively, adds a new field to the known fields of guided tissues regeneration
25 and guided bone regeneration. The preparation of membrane pads having a size of less than 100mm^2 , preferably less than 50mm^2 , from known medical membranes, the modification of the membrane structure and the improved impermeability of the membrane surface facing away from the pulp
30 constitute an essential inventive step which enables the use of membranes with limited permeability in the field of pulp regeneration and dentine regeneration.

Positive practical results were achieved with membrane pads having a thickness of less than 3 mm, preferably less than 0.5 mm. Since thin membranes can have a
35 porosity or density, respectively, which is sufficient

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for dentine regeneration, the use of thin membranes is preferred due to the improved capability of adaptation.

Since the membrane pads are preferably used inside of usually concave cavities or of fracture faces, it is proposed that said membrane pads preferably have an oval or round shape. Such a shaped membrane pad can be optimally arranged in a hemispherical cavity which is the result of dentine caries excavation. A 1 to 2 mm wide seating which is preferably self adhesive on the dentine surrounding the pulpal wound, enables a reliable and provisional impermeable positioning of the membrane.

Preferred is a membrane with a concave or convex shape. The concave, convex or straight variants of the membrane enable depending on the individual case a cupola-like cover of the exposed pulp or a close fit of the membrane to the concavity of the cavity.

In a preferred embodiment the membrane comprises a cover foil which is biologically and chemically impermeable and which preferably fully covers or optionally fully overlaps all sides of the membrane wherein the pad free marginal part of the cover foil which is on the side of the pulp preferably is self adhesive like an adhesive dressing. Said cover foil facilitates the precise positioning of the membrane pad inside a cavity of a tooth. Furthermore, said cover foil allows an impermeable, adhesive connection to the dentine and acts as a barrier towards the suprastructure.

Good results can be achieved with membranes which are made of a non-reabsorbable material such as e.g. polytetrafluoroethylene or preferably titanium. Said membranes are not rejected by the body and titanium is suitable on the one hand for the production of porous structures and on the other hand very good as impermeable material.

Good results can as well be achieved with membranes which are made of reabsorbable material, preferably collagen. Said membranes especially promote at-

tachment and integration of pulp fibroblasts and other regenerative cells and are temporarily sufficiently impermeable to a sealing, hardening material or can be made biologically and chemically impermeable by means of a
5 cover foil.

The membranes are preferably resistant to tearing but can be cut. A soft, sheet-like construction of the membranes makes them arbitrarily deformable and adaptive. Reinforcements of the membrane body or structural modifications can e.g. be achieved by means of titanium lamination or other biologically inert materials. An individual three dimensional shape can be achieved by membranes which e.g. due to reinforcements are plastically deformable ("bleitot").
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The surface of the membrane facing away from the pulp and therefore in contact with the restorative material is preferably inert so that there is no interconnection with the restorative material in order to completely avoid that shrinking forces caused by the polymerization of the restorative material are transferred to the membrane. Said inertia is preferably achieved by teflonisation, hydrophilicity or the use of a non-radically polymer.
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In a further embodiment the surface of the membrane facing away from the pulp and thus in contact with the restorative material forms a mechanical or adhesive bonding to the restorative material in order to assure a impermeable seal of the membrane based pulp capping. Said bonding is preferably achieved by interlocking, entanglement, homo polymerization or copolymerization or secondary or primary chemical bonds. A tight, mechanical and/or adhesive connection to the dental hard tissues, in particular to the dentine, is preferably achieved by means of dentine adhesion, preferably after activation of the adjacent dentine. This can also
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35 be achieved by interlocking, entanglement, homo polymeri-

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zation or co-polymerization as well as secondary or primary chemical bonds.

The inner surface which is in contact with the pulp and thus facing away from the restoration material is preferably biocompatible, promoting attachment or cell integration, respectively, and sterile.

Furthermore, growth factors or bone morphogenic proteins can be added to the membrane or pharmacological effects can be achieved by the membrane such as e.g. soft or hard chemotherapeutical effects which are based on bakteriostatic or bactericidal effects. Finally, tissue stimulating effects leading to e.g. forming of tertiary dentine can be supported by a particular construction of the membrane.

Brief Description of the Drawings

Embodiments of medical membranes according to the invention and their use for the regeneration of the pulp or the regeneration of the dentine are shown in the drawings and are further explained below.

It shows:

Figure 1a a small round membrane with round overlapping carrier foil,

Figure 1b a small round membrane with round carrier foil which has the size of the membrane,

Figure 1c a small round membrane without carrier foil,

Figure 2a a bigger round membrane with a round overlapping carrier foil,

Figure 2b a bigger round membrane with a round carrier foil which has the size of the membrane,

Figure 2c a bigger round membrane without a carrier foil,

Figure 3a a big round membrane with a round overlapping carrier foil,

Figure 3b a big round membrane with a round carrier foil which has the size of the membrane,

5 Figure 4a a small quadratic membrane with a quadratic overlapping carrier foil,

Figure 4b a small quadratic membrane with a quadratic carrier foil with the size of the membrane,

10 Figure 4c a small quadratic membrane without a carrier foil,

Figure 5a an oval membrane with an oval overlapping carrier foil,

Figure 5b an oval membrane with an oval carrier foil which has the size of the membrane,

15 Figure 5c an oval membrane without a carrier foil,

Figure 6a a rectangular membrane with a rectangular carrier foil which has the size of the membrane,

20 Figure 6b a rectangular membrane with a rectangular carrier foil overlapping the membrane,

Figure 6c a rectangular membrane without a carrier foil,

Figure 7 a section through a tooth with a cavity on the right side,

25 Figure 8 a section through a tooth with a big and deep two-faced cavity,

Figure 9 a section through a tooth with a deeper cavity on the right side,

30 Figure 10 a three dimensional drawing of a tooth with a cavity and positioned membrane,

Figure 11 a section through a tooth with positioned membrane and restorative material,

Figure 12 a magnified part of figure 11 and

35 Figure 13 a device for the application of a medical membrane.

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Figures 1 to 6 show different embodiments of membranes 1 to 6. Each of said membrane consists of a porous membrane part 7 to 12 and a dense carrier foil 13 to 18. The carrier foil 13 to 18 is bigger than the membrane part 7 to 12 so that said carrier foil is overlapping the membrane 7 to 12. The carrier foil 13 to 18 can as well have the same size as the membrane 7 to 12 (13' to 18'). Instead of the carrier foil 13 to 18 or 13' to 18', respectively, a coating of the membrane in situ can be used wherein said coating is performed after the primarily adhesive membrane without a carrier foil 7' to 12' has been positioned on the adjacent dentine.

The medical membranes shown in figures 1 to 6 are just embodiments for often used shapes. Depending on the use it is as well possible to apply or use other shapes of medical membranes with or without carrier foils and with or without a suprastructure, respectively.

Said medical membranes 1 to 6 have the function to cover in cavities the area where the pulp is exposed. Examples for such cavities are shown in figures 7 to 9. In figure 7 a cavity 19 of a tooth 20 is shown wherein said cavity cuts in the area 21 the pulp 22. Thereby a sectional plane 23 is formed. In the present case, said sectional plane cuts a circular area of at least 1 to 2 mm width out of the dentine adjacent to the pulp 22 wherein said circular area lies in the plane of sectional plane 23. Said area adjacent to the open pulp serves as contact surface for a membrane 1 to 6.

Figure 8 shows another cavity 24 of a tooth 25 in which the left branch of the pulp 26 is cut. Said cavity 24 has as well around the sectional area 27 of the pulp 26 an at least circular contact surface 28 of dentine.

Figure 9 shows a pulp 30 of a tooth 31 wherein said pulp is cut by a cavity 29. Thereby the sectional plane 32 lies between cavity 29 and pulp 30 in a

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perpendicular plane wherein around the section area 33 an at least circular contact surface 34 of dentine exists.

The formed contact surface around the cut pulp can as well lie transversely in the tooth and can have depending on the situation various shapes. Therefore, there are different, pre-made sterilely packed membrane pads 1 to 6 which have different shapes in order to be applicable in very different situations.

The application of such a membrane pad 1 in cavity 35 of a tooth 36 is shown in more details in figure 10. When the cavity 35 was formed the pulp 38 was cut in the area 37. Thereby a horizontal area 39 around the sectional plane 37 was formed. On said horizontal area 39 the membrane 1 was positioned with the porous membrane part 7 towards the pulp. It has to be observed that the porous membrane part 7 slightly overlaps the contact surface 37 between cavity 35 and pulp 38. The membrane part 7 is then pressed to the area 39 by the carrier foil 13. The bottom side i.e. the side which is in contact with the tooth area 39, of said carrier foil is adhesive or has a structure allowing gluing so that a secure fixation of the applied membrane pad can be provided for.

The sectional drawing of figure 11 shows tooth 36 depicted in figure 10 with an applied membrane pad 1 and above the membrane pad an applied filling 40 in cavity 35. In said figure, the contact of the membrane part 7 with the edge between cavity 35 and pulp 38 can be recognized. The carrier foil 13 lies above the membrane part 7. Said carrier foil is constructed in a way that it can be pressed to the bottom side of the cavity 35 and that it provides for a seal between filling 40 and pulp 38. It is important that the margins of the defect area are sealed by a proper adaptation of the membrane margins in order to prevent lateral penetration of any undesired substances e.g. during the application of hardening sealing material which adheres to the dentine such as e.g.

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light-curing glassionomer cement or during restoration of the defect of the dental hard tissues 40, respectively.

The sectional drawing of figure 12 shows tooth 36 depicted in figure 10 with an applied membrane pad which has a bilayer structure and does not comprise a carrier foil. The seal inside the cavity 35 is primarily provided for by the membrane in the dentine area surrounding the pulp. The membrane is in situ overlaid with a light-curing glassionomer cement 39 which is self adhesive to the dentine of cavity 35. The dentine defect is tightly and adhesively complemented with restoration 40.

Figure 13 shows a device 40 for the application of a medical membrane 1 in a dentine cavity 41 of a tooth 42 which cuts pulp 43. The device 40 comprises a handle 44 to which a skeleton form 45 is removably fixed. The skeleton form 45 has preferably a shape which corresponds to the shape of a cavity e.g. hemispherical or plane in order to allow pressing of the medical membrane so that there is no marginal gap and an overlaying with e.g. a light-curing glassionomer cement is possible. In a preferred embodiment the skeleton form 45 is made of a material e.g. composite, ceramic or a polymer which after hardening remains in the cavity and becomes part of the filling. The skeleton form 45 is fixed in such a way to the handle 44 of the device so that it can easily be attached or removed by the operator.

The desired diameter of the pulp pads 1 to 6 is between 1 mm and 10 mm depending on the size of the cross section of the pulp or cavity, respectively. For a sufficient circular sealing an about 1 to 2 mm wide zone around the open pulp is necessary. Thereby, any contact at the marginal zone of the open pulp with foreign and toxic substances should be a priori prevented.

After a certain time, the applied membranes are „immured“ between the overlaying material or the filling, respectively, and the tertiary dentine freshly formed on the side which is in contact with the pulp or

said membranes are in the course of time reabsorbed. The tightly enclosed membrane pad can remain in situ indefinitely and forms part of the filling.

The bottom side of the pulp pad corresponds
5 to the structure of known medical membranes wherein an average diameter of the pores between 1 μm and 100 μm and a percentage of pores of more than 50 % are preferred. Said diameter of the pores offers to the regenerative cells and to the extracellular substances such as e.g.
10 fibrin an impermeable support during the whole healing process. Along the fibrin fibers regenerative cells reach the surface of the membrane.

The successful treatment depends on sterile surgical work i.e. that the work is performed without a
15 bacteria burden for the pulp and that the pulp is only in contact with the sterile membrane and that it has no contact with filling material or that it is not exposed to microorganisms penetrating from outside. Furthermore, it is important that the porous membrane part fits tightly
20 to the dentine. Depending on the shape of the cavity the membrane can be applied to the pulp either as a convex or a concave membrane, respectively. Preferred is a membrane according to the present invention which is packed sterilely in order to allow sterile work.

25 The described membrane pads are of crucial importance for the medical treatment of teeth since hitherto no primary wound healing of pulp exposures could be achieved. Nowadays, the pulp is overlaid with $\text{Ca}(\text{OH})_2$ which causes in the pulp tissue lying below a harmful necrosis and protected by said necrosis tertiary dentine is
30 formed in the context of a inflammation reaction. This is only possible in young patients whose pulp has a good ability to regenerate. Since the pulp does not have a collateral circulation and since it is only capable of a
35 limited defense response, the limited defense response of the pulp can not cope with bigger wound areas. In older

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patients the number of dentine forming stem cells is very small and therefore the treatment was often unsuccessful.

The membrane pads according to the present invention create inside a tooth ideal preconditions for a primary wound healing of the exposed pulp. The sterile, impermeable seal, the absence of a wound treatment harming the pulp, the wound healing stimulating structure, the mechanical stability and the possibility to tightly close the edges of the wound and to complement the dentine defect immediately make it possible that even pulp exposures with a big wound area or more than one wound area can be treated successfully.

While there are shown and described presently preferred embodiments of the invention, it is to be distinctly understood that the invention is not limited thereto but may be otherwise variously embodied and practiced within the scope of the following claims.

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